## AMENDMENT

**Amendments to the Claims**

1. (currently amended) A phospholipid nanovesicle incorporating a polypeptide comprising

a phospholipid selected from the group consisting of phosphatidylserine, phosphatidylethanolamine and structural analogs thereof,

an isolated saposin C-related polypeptide, wherein the polypeptide is selected from the group consisting of: (a) a polypeptide having an amino acid sequence at least 95 percent identical to SEQ ID NO: 2; (b) a polypeptide having an amino acid sequence as set forth in SEQ ID NO: 2 and having one or more conservative substitutions; and (c) a polypeptide having an amino acid sequence identical to SEQ ID NO: 2;

and a pharmaceutically acceptable carrier;

wherein the polypeptide comprises a saposin fold ~~H1 through H5 helix regions of saposin C~~ and retains plasma membrane affinity;

wherein the phospholipid forms a nanovesicle having the polypeptide embedded within

wherein the phospholipid forms a nanovesicle having the polypeptide embedded within the phospholipids of the ~~its polypeptide embedded~~ nanovesicle;

and wherein the nanovesicle exhibits anti-tumor activity.

2. (previously presented) The composition of claim 1, wherein the phospholipid is phosphatidylserine or a structural analog thereof.

3. (previously presented) The composition of claim 2, wherein said phosphatidylserine or structural analog thereof is selected from the group consisting of phosphatidic acid, phosphatidylglycerol, phosphatidylinositol, palmitoyloleoylphosphatidylserine, palmitelaidoyloleoylphosphatidylserine, myristoleoyloleoylphosphatidylserine, dilinoleoylphosphatidylserine, palmiticlinoleoylphosphatidylserine, lysophosphatidylserine, and

dioleoylphosphatidylserine.

4. (previously presented) The composition of claim 1, wherein the molar ratio of polypeptide to phospholipid is in the range from about 1:1 to about 1:50.

5. (previously presented) The composition of claim 2, wherein the molar ratio of saposin C-related polypeptide to phospholipid is in the range from about 1:1 to about 1:10.

6. (previously presented) The composition of claim 1 wherein the composition is capable of inducing apoptosis in hyper-proliferating cells.

7. (previously presented) The composition of claim 1, wherein the polypeptide comprises at least 80 contiguous amino acids SEQ ID NO: 2.

8. (previously presented) The composition of claim 7, wherein the mass ratio of the polypeptide to the phospholipid is in the range from about 15:1 to about 3:10.

9. (withdrawn) A method for modulating the distribution of an inner leaflet component in a plasma membrane of a cell of a subject comprising administering to said subject a therapeutically effective amount of the agent of claim 1.

10. (withdrawn) A method for modulating the distribution of an inner leaflet component in a plasma membrane of a cell of a subject comprising administering to said subject a therapeutically effective amount of the agent of claim 1.

11. (withdrawn) The method of claim 9, wherein said inner leaflet component is phosphatidylserine or a structural analog thereof.

12. (withdrawn) The method of claim 10, wherein said phosphatidylserine or structural analog thereof is dioleoylphosphatidylserine.

13. (withdrawn) The method of claim 9, wherein the distribution of said inner leaflet component in the outer leaflet of said plasma membrane is altered.

14. (withdrawn) The method of claim 12, wherein the concentration of said inner

leaflet component in said outer leaflet is increased.

15. (withdrawn) The method of claim 9, wherein the distribution of said inner leaflet component is modulated in hyper-proliferating cells.

16. (withdrawn) The method of claim 14, wherein said hyper-proliferating cells are selected from the group consisting of tumor cells and cancer cells.

17. (withdrawn) The method of claim 9, wherein said method promotes cell death.

18. (withdrawn) A method of modulating tumor volume in a subject, said method comprising administering a therapeutically effective amount of the agent of claim 1.

19. (withdrawn) The method of claim 17, wherein said agent promotes cell death in hyper- proliferating cells.

20. (withdrawn) The method of claim 18, wherein said hyper-proliferating cells are selected from the group consisting of tumor cells and cancer cells.

21. (withdrawn) The method of claim 19, wherein said cancer cells are selected from the group consisting of sarcoma, neuroblastoma, breast carcinoma, and squamous cell carcinoma cells.

22. (withdrawn) The method of claim 17, wherein said inner leaflet component is phosphatidylserine or a structural analog thereof.

23. (withdrawn) The method of claim 21, wherein said phosphatidylserine or structural analog thereof is dioleoylphosphatidylserine.

24. (withdrawn) The method of claim 17, wherein said subject is a mammal.

25. (withdrawn) The method of claim 23, wherein said mammal is a human.

26. (withdrawn) The method of claim 17, wherein said tumor volume decreases.

26. (withdrawn) The method of claim 17, wherein the molar ratio of said polypeptide to said inner leaflet component is in the range from about 1:1 to about 1:50.

27. (withdrawn) The method of claim 26, wherein the molar ratio of said polypeptide to said inner leaflet component is in the range from about 1:1 to about 1:10.

28. (withdrawn) The method of claim 17, wherein said agent further comprises a pharmaceutically acceptable carrier.

29. (withdrawn) A method of treating a cancer in a subject, said method comprising administering a therapeutically effective amount of the agent of claim 1.

30. (withdrawn) The method of claim 29, wherein said inner leaflet component is phosphatidylserine or a structural analog thereof.

31. (withdrawn) The method of claim 30, wherein said phosphatidylserine or structural analog thereof is dioleoylphosphatidylserine.

32. (withdrawn) The method of claim 29, wherein the molar ratio of said polypeptide to said inner leaflet component is in the range from about 1:1 to about 1:50.

33. (withdrawn) The agent of claim 32, wherein the molar ratio of said polypeptide to said inner leaflet component is in the range from about 1:1 to about 1:10.

34. (withdrawn) The method of claim 29, wherein said agent further comprises a pharmaceutically acceptable carrier.

35. (withdrawn) The method of claim 29, wherein said agent promotes cell death in hyper-proliferating cells.

36. (withdrawn) The method of claim 35, wherein said cell death occurs through apoptosis.

37. (withdrawn) The method of claim 35, wherein said hyper-proliferating cells are selected from the group consisting of cancer cells.

38. (withdrawn) The method of claim 37, wherein said cancer cells are selected from the group consisting of sarcoma, neuroblastoma, breast carcinoma, and squamous cell carcinoma cells.

39. (withdrawn) The method of claim 29, wherein said subject is a mammal.

40. (withdrawn) The method of claim 39, wherein said mammal is a human.

41. (withdrawn) The method of claim 29, wherein said agent is administered enterally, parenterally, subcutaneously, intravenously, intraperitoneally, or topically.

42. (withdrawn) The method of claim 29, wherein multiple doses of said agent are administered to said subject.

43. (withdrawn) The method of claim 29, wherein a single dose of said agent is administered to said subject.

44. (withdrawn) An anti-tumor composition comprising a nanovesicle prepared by the process of claim 64, wherein the polypeptide has the amino acid sequence set forth in SEQ ID NO:2, wherein the inner leaflet component is dioleoylphosphatidylserine and wherein the composition is capable of inducing apoptosis in hyper-proliferating cells.

45. (withdrawn) The anti-tumor composition of claim 44, wherein the mass ratio of polypeptide to dioleoylphosphatidylserine is approximately 5:1.

46. (withdrawn) The anti-tumor composition of claim 44, wherein the mass ratio of polypeptide to dioleoylphosphatidylserine is approximately 15:7.

47. (withdrawn) The anti-tumor composition of claim 44, wherein the mass ratio of polypeptide to dioleoylphosphatidylserine is in the range from about 15:1 to about 3:10.

48. (withdrawn) The anti-tumor composition of claim 44, comprising approximately 10 μM polypeptide and approximately 30 μM dioleoylphosphatidylserine.

49. (withdrawn) The anti-tumor composition of claim 44, comprising approximately 10 μM polypeptide and approximately 70 μM dioleoylphosphatidylserine.

50. (currently amended) A composition consisting essentially of an anionic phospholipid nanovesicle consisting of phosphatidylserine or structural analog thereof embedded with a biologically active saposin C-related polypeptide, wherein the polypeptide comprises an

amino acid sequence that (i) has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:2 or (ii) differs by one or more conservative amino acid substitutions from the amino acid sequence of SEQ ID NO:2; and a pharmaceutically acceptable carrier; wherein the polypeptide includes sequences which form a saposin fold ~~helix regions H1 and H5 of saposin C~~, which embed within the lipid bilayer of the nanovesicle, and wherein the polypeptide -embedded phospholipid nanovesicle exhibits anti-tumor activity.

51. (previously presented) The composition of claim 50, wherein the phospholipid is phosphatidylserine or a structural analog thereof.

52. (previously presented) The composition of claim 51, wherein the phospholipid is a phosphatidylserine selected from the group consisting of palmitoyloleoylphosphatidylserine, palmitelaidoyloleoylphosphatidylserine, myristoleoyloleoylphosphatidylserine, dilinoleoylphosphatidylserine, palmiticlinoleoylphosphatidylserine, lysophosphatidylserine, and dioleoylphosphatidylserine.

53. (previously presented) The composition of claim 51, wherein the molar ratio of polypeptide to phospholipid is in the range from about 1:1 to about 1:50.

54. (previously presented) The composition of claim 51, wherein the molar ratio of polypeptide to phospholipid is in the range from about 1:1 to about 1:10.

55. (previously presented) The composition of claim 51 wherein the composition is capable of inducing apoptosis in hyper-proliferating cells upon contact.

56. (previously presented) The composition of claim 51, wherein the polypeptide comprises an amino acid sequence that differs by 5 or fewer conservative amino acid substitutions from the amino acid sequence of SEQ ID NO:2 .

57. (previously presented) The composition of claim 56, wherein the mass ratio of the polypeptide to the phospholipid is in the range from about 15:1 to about 3:10.

58. (withdrawn) A process for the manufacture of a pharmaceutical composition comprising the steps of:

(a) combining a composition comprising (i) an inner leaflet component, wherein the inner leaflet component is a phospholipid selected from the group consisting of phosphatidylserine, phosphatidylethanolamine and structural analogs thereof and (ii) a prosaposin-related polypeptide;

wherein the polypeptide has an amino acid sequence selected from the group consisting of the amino acid sequence set forth in SEQ ID NO:1, a biologically active variant of the amino acid sequence set forth in SEQ ID NO:1, the amino acid sequence set forth in SEQ ID NO:1 having one or more conservative substitutions, the amino acid sequence set forth in SEQ ID NO:2, a biologically active variant of the amino acid sequence set forth in SEQ ID NO:2, and the amino acid sequence set forth in SEQ ID NO:2 having one or more conservative substitutions and wherein the polypeptide retains plasma-membrane affinity;

in a pharmaceutically acceptable carrier;

(b) treating the suspension of inner leaflet component and prosaposin-related polypeptide to form a nanovesicle;

wherein the nanovesicle formed exhibits anti-tumor activity.

59. (withdrawn) A pharmaceutical composition comprising nanovesicles prepared by the process of claim 58.

60. (withdrawn) The pharmaceutical composition of claim 59, wherein the polypeptide has an amino acid sequence selected from the group consisting of the amino acid sequence set forth in SEQ ID NO:1, the amino acid sequence set forth in SEQ ID NO:1 having one or more conservative substitutions, the amino acid sequence set forth in SEQ ID NO:2, and the amino acid sequence set forth in SEQ ID NO:2 having one or more conservative substitutions.

61. (withdrawn) The pharmaceutical composition of claim 60, wherein the inner leaflet component is phosphatidylserine or a structural analog thereof.

62. (withdrawn) The pharmaceutical composition of claim 61, wherein

the molar ratio of polypeptide to phospholipid is in the range from about 1:1 to about 1:50.

63. (withdrawn) The pharmaceutical composition of claim 62, wherein the nanovesicle has a diameter in the range 0.01 to 1 μm.

64. (withdrawn) A process for the manufacture of a pharmaceutical composition comprising the steps of:

(a) combining a composition comprising (i) a dried inner leaflet component, wherein the inner leaflet component is phosphatidylserine or a structural analog thereof and (ii) a dried and isolated prosaposin-related polypeptide;

wherein the polypeptide has an amino acid sequence selected from the group consisting of the amino acid sequence set forth in SEQ ID NO:1, the amino acid sequence set forth in SEQ ID NO:1 having one or more conservative substitutions, the amino acid sequence set forth in SEQ ID NO:2, and the amino acid sequence set forth in SEQ ID NO:2 having one or more conservative substitutions and wherein the polypeptide retains plasma-membrane affinity;

wherein the molar ratio of the polypeptide to the inner leaflet component in the composition is in the range from 1:1 to 1:25;

in a pharmaceutically acceptable carrier;

(b) treating the suspension of inner leaflet component and prosaposin-related polypeptide to form a nanovesicle;

wherein the nanovesicle formed has a diameter in the range 10 to 800 nm and exhibits anti-tumor activity.

65. (withdrawn) A pharmaceutical composition comprising nanovesicles prepared by the process of claim 64.